Published Abstract in ECTRIMS 2006

Clinical aspects: diagnosis and differential diagnosis - Part II

Friday, September 29, 2006, 15:30 - 17:00

A panel of anti-glycan IgM antibodies for predicting the development of relapsing-remitting multiple sclerosis after the first neurological event

M.S. Freedman, A. Miller, M. Schwarz, 0. Weisshaus, R.T. Allstock, A. Duker, N. Dotan, C. Sindic (Ottawa, CAN; Haifa, Lod, IL; Brussels, B)

Background: There is an unmet need to develop specific serum based biomarkers for the diagnosis and prognosis of Relapsing Remitting MS (RRMS). We have reported that elevated levels of serum anti-Glc(alphal ,4) Glc(alpha) (GAGA4) IgM antibodies (Ab) exist in RRMS patients in comparison to patients with other neurological diseases (OND) enabling to discern which post-CIS patients convert to RRMS vs. OND. We have further investigate whether other anti glucose based IgM Ab may improve on the RRMS prediction for CIS patients. Aim: To evaluate the predictive value of IgM Ab against Glc(alpha1,6)Glc(alpha) (GAGA6), alpha-GlcNAc (GNa) , and GAGA4, for identifying patients with CIS that will evolve to RRMS or will have a more active disease. Methods: Retrospective analysis on of 88 frozen sera from CIS patients presenting for diagnostic work-up and were followed for a minimum of 4 years, Forty four patients were subsequently confirmed to have RRMS, whereas the other 44 developed OND (other inflammatory (OIND), n=23, or non-inflammatory neurological disease (ONIND), n=21). The groups were matched for gender composition, age and total IgM. Sera were diluted 1:1200 and levels of GAGA6, GAGA4 and GNa IgM Ab measured by enzyme immunoassay normalized to IgM levels. Results: Significantly higher levels of anti-GAGA6 IgM (p=0.01) and anti-GAGA4 IgM (p=0.005) Ab were observed in CIS patients who converted to RRMS as opposed to OND. Using the OND sample set and a cut-off of mean + 280 for anti GAGA6 and GAGA4, we have found that 17144 (39%) converting CIS patients were positive, whereas 42144 (95%) OND patients were negative for both Ab, corresponding to a sensitivity of 39%, a specificity of 95%, PPV of 89%, and NPV of 61%. In addition, higher levels of anti-GAGA4 and anti-GNa Ab (g. median) predicted a greater number of future attacks. RRMS patients with levels > median vs. patients with lower levels (< median) of antiGAGA4 and anti-GNa IgM antibodies went on significantly (16/20 (80%) vs. 10121 (47%), and 17120 (85%) vs. 9/21 (43%), (f02 test, p=0.025) odds ratio 4.4 (CI 95% 1.6-11.8), and odds ratio 7.5 (CI 95% 2.4-23.8), respectively to have further attacks within 2 years.

Conclusion: Measuring Anti-GAGA4 together with Anti-GAGA6 IgM yields higher sensitivity (39%), specificity (95%) and PPV (89%) of CIS patients evolving to RRMS. In Addition higher levels of IgM antibodies to the GAGA4 and GNa epitopes predicts at CIS which patients Will have imminent attacks.